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Article

Disability-Adjusted Life Year Frameworks for Comparing Health Impacts Associated with *Mycobacterium avium*, Trihalomethanes, and Haloacetic Acids in a Building Plumbing System

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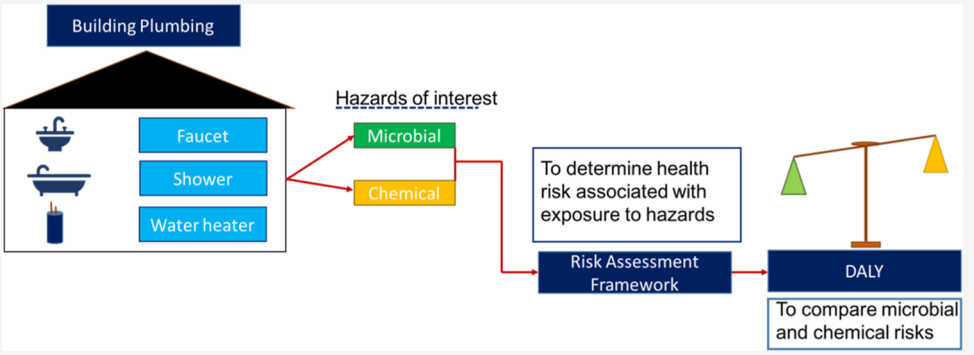

ABSTRACT: To address trade-offs, prioritize, and manage the risks between microbial and chemical risks, the disability-adjusted life year (DALY) approach was utilized. The sampling data from cold and hot water building plumbing in Philadelphia, PA, revealed three classes of health stressors, nontuberculous mycobacteria, total trihalomethanes (THMs), and total haloacetic acids (HAAs). The concentration data specific to the water system were then used to estimate the annual risk due to the *Mycobacterium avium* complex (MAC), THMs, and HAAs. The results from this study suggest that efforts to reduce the potential health risks from disinfection byproducts should still be given due consideration as the annual DALY of bladder cancer ($7.61*10^{-7}$) was estimated to be greater than the annual DALY of MAC pulmonary disease ($4.74*10^{-12}$) by 5 orders of magnitude. The DALYs of both THMs ($2.62*10^{-6}$) and HAAs ($2.60*10^{-6}$) in buildings via the ingestion exposure route were higher than the reported threshold of 1 μDALY. Relative to the feed water, water quality changes in the building plumbing substantially increased the DALY impacts for microbial risks but modestly decreased the DALY impacts for chemical risks. While the results are specific to the system considered (e.g., chloramine disinfectant, no detectable *Legionella*), the study presents a framework for prioritizing among building plumbing microbial and chemical risks.

KEYWORDS: *risk assessment, Mycobacterium avium, trihalomethanes, haloacetic acids, building plumbing, drinking water quality*

1. INTRODUCTION

Building plumbing—the portion of water distribution system between the water main and final points of exposure—raises emerging concerns for water quality as the conditions in building plumbing, such as plumbing materials, temperature, pH, water flow patterns, and low chlorine residual levels may present both microbiological and chemical hazards.[1−6] Residual disinfectant is generally provided in U.S. water supplies to protect against microbial (re)growth, presence, and colonization. Common microbial concerns include exposure to opportunistic pathogens such as *Legionella*, pathogenic nontuberculous mycobacteria (NTM) species, and *Pseudomonas aeruginosa*. Chemical concerns include the reaction between disinfectants and organic matter to form potentially carcinogenic disinfection byproducts (DBPs) including trihalomethanes (THMs), haloacetic acids (HAAs), haloacetonitriles, haloketones, and other known and unknown byproducts.[7,8]

Exposure to both microbial and chemical contaminants in building water has led to an increasing interest in the application of quantitative risk assessment for both chemical and microbial hazards.[9−11] Previously, risk assessment studies were conducted to better understand the exposure risks of water contaminants including opportunistic pathogens and DBPs by several different exposure scenarios and routes.[12−19]

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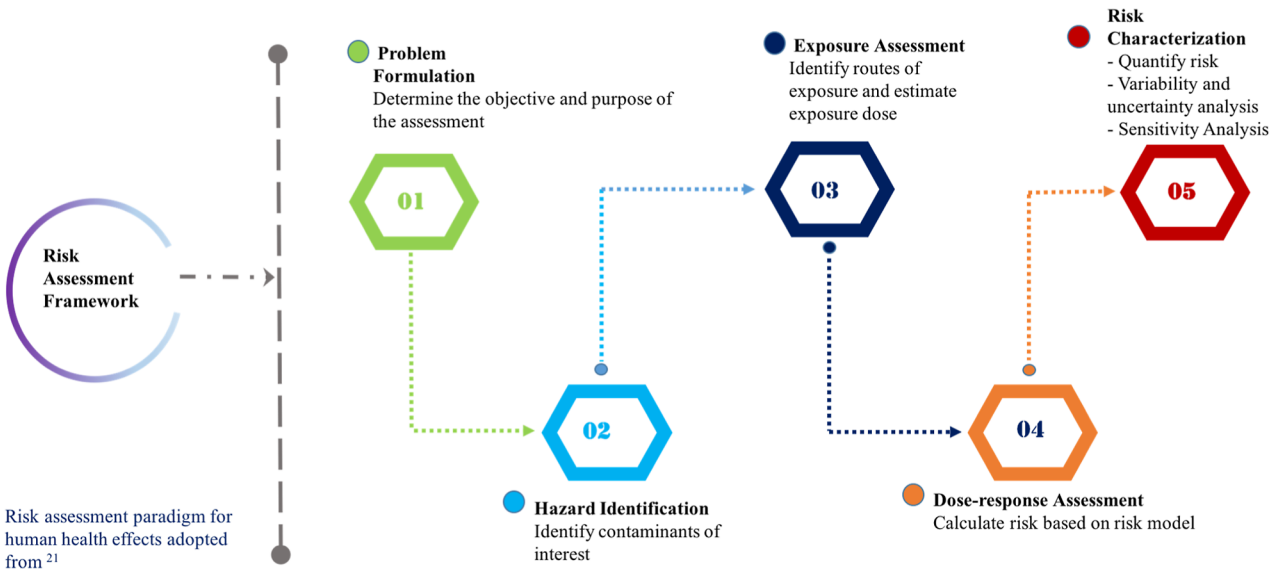

Figure 1. Risk assessment framework for human health effects.

Although these studies have provided insights, particularly with regard to the acceptable concentration limits of some pathogens in drinking water and the development of dose−response models for MAC, to the authors' knowledge, there are currently few studies that compare chemical and microbial health risks[20,21] but not under building plumbing conditions.

In this study, QMRA and chemical risk assessments were performed to assess and compare microbial and chemical risks given site-specific monitoring of water quality. The specific objectives of this study are (1) to quantify the risk of infection from exposure to MAC using the QMRA framework, (2) to estimate the cancer risk due to regulated DBPs (THMs and HAAs) using the chemical risk assessment framework, (3) to establish a framework for comparing health burdens from exposure to MAC and the different disinfectant byproducts using the disability-adjusted life years (DALY) approach, and (4) to apply this framework to monitoring data from model hot and cold water systems in Philadelphia, PA, where chloramine is the secondary disinfectant type used. While the results cannot be considered representative of national exposures, they do show the impact of a range of different plumbing conditions (residence times, water heater temperatures, blends of hot and cold water, etc.) on risks.

2. METHODS

2.1. Overview of Risk Analysis. This study uses the quantitative risk assessment for both microbial and chemical contaminants adopted from ref 22. Figure 1 outlines the various components that make up the overall framework and how it is applied in this study. The framework consists of hazard identification, exposure assessment, dose−response assessment, and risk characterization.

2.2. Hazard Identification. *2.2.1. Pathogens of Interest.* NTM were the only opportunistic pathogens consistently found in the sampling data,[23] and for this reason as well as its potential health issues, NTM are the pathogens of interest in this study. NTM are a large diverse group of species in the *Mycobacterium genus,* and *Mycobacterium abscessus* complex, *Mycobacterium kansasii*, *Mycobacterium intracellular,* and *Mycobacterium avium* complex (MAC) are among the most frequent species that are recognized as important human pathogens.[24,25] Various disease outcomes are associated with MAC, including pulmonary disease, soft tissue infections, disseminated infections, cervical lymphadenitis in immune-competent patients,[26,27] and fibronodular disease with bronchiectasis, also known as "Lady Windermere's Syndrome".[28]

The concentration data of NTM were taken from previous studies conducted in cold water plumbing pipes[6] and hot water heater storage tanks.[23] As a conservative assumption, NTM is assumed to be 100% MAC in this study. The studies were conducted in Philadelphia, where monochloramine is used as a secondary disinfectant. In this study, the risk analysis for MAC via inhalation is conducted for three different water use scenarios. The first scenario calculates exposure based on concentrations in the building influent or feed, as measured in ref 23, which is fresh water from the water supply distribution system sampled after 15 min of flushing at the tap. In using this concentration to characterize exposure from a shower, one assumes that water is brought up from the water supply temperature of approximately 25 °C to an appropriate temperature for showering without substantial growth or attenuation of concentrations. The second scenario is referred to as the blend which is a mixture of 67% hot water, with concentrations taken from the hot water tank experiment,[23] and 33% cold water, with concentrations taken from the cold water study[6] in which stagnation was allowed for either 12 h or 1 week prior to sampling. This mixture would have a temperature of roughly 40 °C and represents a scenario where some degree of influence from the building plumbing system is present in both hot and cold water. The third scenario is termed the water heater scenario, which is based solely on the hot water tank experimental data[23] based on the weighted average of the different experimental conditions studied consisting of 85% of the values at 48 °C and 15% of the values at 60 °C for a final temperature of 49.8 °C. This scenario avoids the possible disproportionate impact of the first flush from the cold water system which comprises 33% of the data in the "blend" scenario. The fourth scenario consisting of a mixture of water from the water heater tank and cold water not allowed to stagnate can readily be calculated as the weighted average of the feed and the water heater data.

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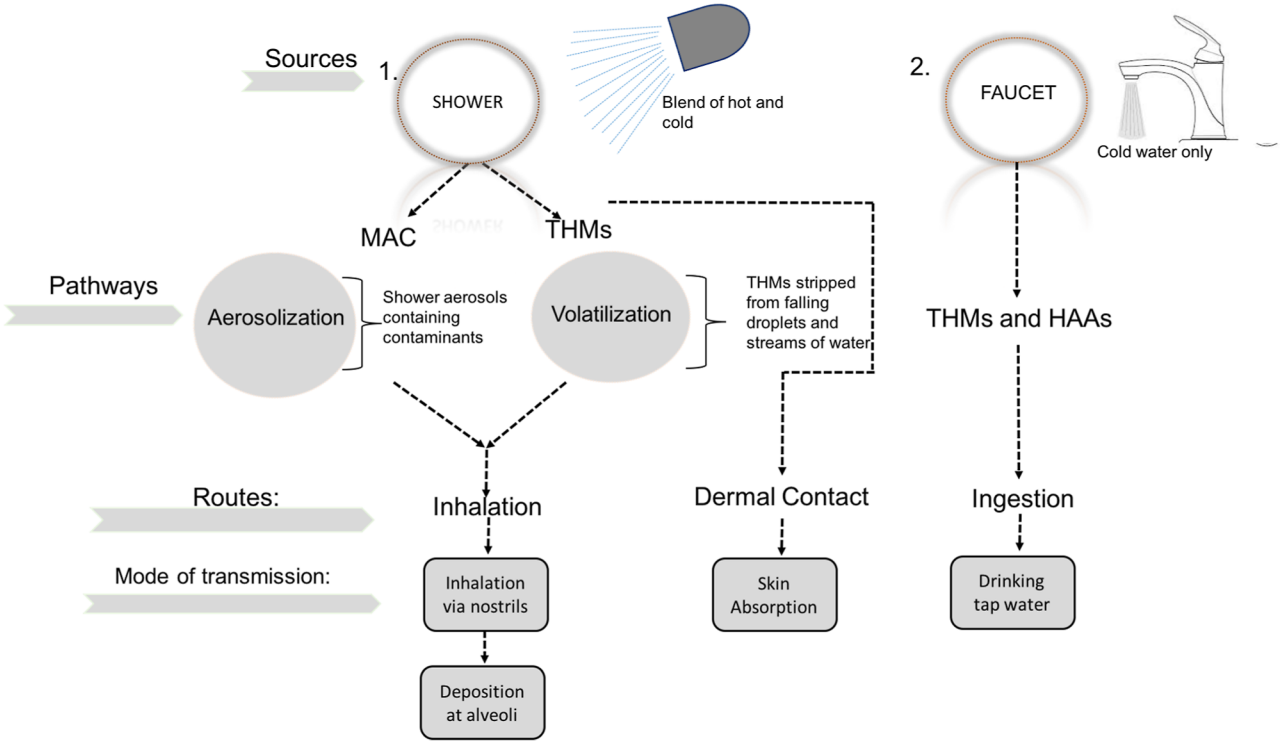

Figure 2. Conceptual model showing the different pathways, exposure routes, and mode of transmission considered for MAC and DBP risk assessment in this study.

2.2.2. Chemicals of Interest. The regulated DBPs of interest in this study consist of four THMs—chloroform (CFM), bromoform (BFM), dibromochloromethane (DBCM), and bromodichloromethane (BDCM)−−and three of the five regulated HAAs—dibromoacetic acid (DBAA), dichloroacetic acid (DCAA), and trichloroacetic acid (TCAA). The other two HAAs, monobromoacetic acid and monochloroacetic acid, are considered noncarcinogenic and are not considered in this study. THMs and HAAs are the two major groups of DBPs among the known specific DBPs that are formed by the chlorination of natural waters.[8,29,30] Due to their potential health risks, as well as their role as surrogates for the control of other halogenated DBPs of health concern, they are the chemical contaminants of interest in this study.

The measurements of total THMs and HAAs are described elsewhere.[31] The concentrations of individual THM species and the species of the five regulated HAAs were estimated based on the average fractions of individual THM and HAA species measured in the water treatment plant serving the Philadelphia area and were provided by the Philadelphia Water Department. The information on the percent concentration for the three treatment plants and the concentrations of the total THMs measured during the hot water storage tank experiment reported in ref 31 are provided in the Supporting Information. For the inhalation exposure route, THMs were the only DBPs considered, as HAAs are reported to have low volatility and inhalation risks for these compounds are not considered to be of great concern.[32] The exposure scenarios are like those considered for the MAC inhalation exposure.

The cold water DBP concentrations were estimated from the total THM and HAA values measured from the cold water pipe rack experiments reported in ref 33 and the speciation data from the Philadelphia Water Department. The risk analyses for THMs and HAAs via ingestion are conducted for multiple scenarios. The first uses concentrations from the feed which is nonstagnant influent water to the building from the service line. The second uses concentrations from the first flush samples of water from the pipes that had stagnated in the building plumbing. The remaining scenarios present results separately for water that stagnated in the pipes of different materials (PEX, PVC, and copper) and use frequency (high use = 12 h of stagnation, and low use = 1 week of stagnation). The low water use scenario is assumed to be a scenario where someone drinks every day from a tap which is used only once a week (i.e., this is an extreme scenario for exposure to stagnant water as the exposed individual would have to rotate the taps used on different days).

2.3. Exposure Assessment. Figure 2 shows the conceptual exposure model for both MAC and DBPs. For MAC, the conceptual model illustrates exposure from the inhalation of shower aerosols containing biofilm-associated MAC detached from premise plumbing. While NTM species grow in biofilms attached to pipe walls, they periodically detach from the pipe walls and can be found in the water column. In this study, NTM concentrations were measured in the water column not in the biofilm. MAC is then aerosolized after flowing through the shower head. Once inhalation takes place, only a fraction of the inhaled bacteria reaches the alveolar region, which is referred to as the deposited dose. For the DBPs, the conceptual model illustrates exposure via the inhalation of volatilized species of DBPs during a warm shower in an enclosed shower room and ingestion of tap water.

2.3.1. Exposure Scenarios, Routes of Concerns, and Population of Interest. The exposure routes of concern for the shower scenario are inhalation (MAC and THM) and dermal contact (THM and HAA). The second exposure scenario of concern is oral ingestion of faucet water, where THMs and HAAs are the contaminants of concern. MAC is

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not considered in the ingestion scenario as the available dose−response model for MAC ingestion is specific for immunocompromised individuals and not the general public, which is the main population of interest in this study. The comparative analysis in this study would not be applicable to immunocompromised individuals who are subject to ingestion risk from MAC.[34]

The exposure scenarios, routes, and health endpoints considered in this study are summarized in Table 1. To obtain a representative risk distribution, the computations were performed with 10,000 Monte Carlo simulations for each studied area using R version 3.00 (www.rproject.org), which was verified to be sufficient to yield a stable estimate of risk, and the seed was set using (123).

Table 1. Overview of the Type of Risk Assessment for the Different Exposure Routes and Scenarios and Health Endpoints

type of assessment	exposure scenario	exposure route	index of concern	health endpoint
microbial assessment	showering	inhalation	MAC	pulmonary disease
chemical cancer assessment	showering	inhalation	THM	bladder cancer
	showering	dermal contact	HAAs and THMs	liver cancer
	consumption of tap water	ingestion	HAAs and THMs	liver cancer

2.3.2. Exposure Models. 2.3.2.1. Inhalation Exposure Model for MAC. The inhalation exposure model is based on ref 35 and is used to estimate the inhaled dose of MAC via showering for a general population

$$D_{\text{inh}} = C_{\text{MAC}} \times B \times t \times E \times \sum_{i=1}^{10} (C_{\text{aer},i} \times V_{\text{aer},i} \times D_i) \quad (1)$$

where D_{inh} is the exposure dose from inhalation, C_{MAC} is the concentration of MAC at the shower head (cfu/m^3); for this analysis, the concentration of MAC is assumed to be based on 100% of the NTM concentration, B is the breathing rate (m^3/min), t is the exposure duration (min), E is the enrichment factor (dimensionless) that refers to the ratio of bacteria concentration in the ejected bioaerosol droplets (#/L water droplets) to the concentration in the same volume of bulk water (#/L bulk water), $C_{\text{aer},i}$ is the concentration of aerosols (#/m^3) of diameter i, where i is in the range of 1−10 μm, $V_{\text{aer},i}$ is the volume of each aerosol particle (m^3) for the size bin (diameter) i calculated as $V = \pi/6(i*10^{-6})^3$, and D_i is the alveolar deposition efficiency of size i diameter aerosols.

2.3.2.2. Inhalation Exposure Model for THMs. The model used to calculate the inhalational exposure to THMs volatilized into the shower room is based on the updated EPA inhalation risk assessment guide. The updated methodology recommends that risk assessors use the concentration in air (C_{air}) as the exposure metric (e.g., mg/m^3) instead of the intake of a contaminant in air based on the inhalation rate and body weight (e.g., mg/kg/day). The equation is given as

$$\text{EC} = (C_{\text{air}} \times \text{ET} \times \text{EF} \times \text{ED})/(\text{AT}) \quad (2)$$

where EC is the exposure concentration (mg/m^3), ET is the exposure time (min/day), EF is the exposure frequency (day/year), ED is the exposure duration (year), and AT is the average exposure time (year).

The air concentration is estimated based on the two resistance theories applied to the transfer of volatile contaminants from the shower water to indoor air by means of two transient mass balance models developed in ref 36. The estimation includes Henry's constant which describes the solubility of gases in liquids. Henry's constants for different water temperatures used in this study for all the four species of THMs were calculated based on the equations from ref 37 and compared to the values from the literature. Henry's constants were converted to dimensionless values by dividing the values obtained by the absolute temperature (T = 298.15 K) and the constant of the ideal gas (R = 8.21*10^{-5} m^3 atm K^{-1} mol^{-1}).[38]

2.3.2.3. Ingestion Exposure Model for THMs and HAAs. The ingestion dose is given by

$$\text{CDI}_{\text{oral}} = (\text{CW} \times \text{IR} \times \text{EF} \times \text{ED})/(\text{BW} \times \text{AT}) \quad (3)$$

where CW is the chemical concentration in water (mg/m^3), IR is the ingestion rate (m^3/day), EF is the exposure frequency (days/year), ED is the exposure duration, (years), BW is the body weight (kg), and AT is the average time (years).

2.3.2.4. Dermal Absorption Exposure Model for THMs and HAAs. The dermal dose is given by

$$\text{CDI}_{\text{Dermal}} = (\text{CW} \times \text{SA} \times \text{PC} \times \text{ET} \times \text{EF} \times \text{ED} \times \text{CF})/(\text{BW} \times \text{AT}) \quad (4)$$

where CW is the chemical concentration in water (mg/m^3), SA is the area of body exposed to water during showering (m^2), PC is the species-specific dermal permeability constant (cm/h), ET is the exposure time (min/day), EF is the exposure frequency (days/year), ED is the exposure duration (year), CF is the conversion factor from cm/h to m/min which is equivalent to 1.67*10^{-4}, BW is the body weight (kg), and AT is the average time (years).

The input parameters for both MAC and DBP exposure assessment that were deterministic include the measured concentrations of MAC, THMs, and HAAs, exposure frequency, exposure duration, body weight, water flow rate, and air flow rate. The parameters that were treated stochastically include breathing rate, exposure time, concentration of aerosols, inhalation rate, exposure time, bathroom volume, and ingestion rate.

2.4. Dose−Response Assessment. For estimating the risk of MAC exposure for the general population through inhalation with an endpoint of pulmonary disease, the exponential model is considered the preferred model

$$P_{\text{response}} = 1 - e^{-rd} \quad (5)$$

where r is the probability of an organism surviving and reaching the appropriate site to initiate infection, d is the organism dose, and P_{response} is the probability of the relevant endpoint, which in this study is the probability of illness (as illness rather than infection was used to fit the dose−response model). A study performed in ref 39 estimated the parameter r based on data from mice with an intravenous exposure route which is not representative of the human exposure scenario being considered in this study. Another study proposed including a conversion factor or distribution of conversion factors to the model as a parameter to extrapolate from intravenous exposure to the desired human exposure.[35]

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Table 2. MAC Inhalation Exposure Pathway Based on Water Heater Data or Blended Hot−Cold Water Based on Average Concentration Data from Hot Water Experiment Study Described in Reference 23 and Pipe Rack Experiment in Reference 6

exposure scenario	daily exposure dose, cfu (90% probability interval)	daily probability of illness, (90% probability of illness)	annual probability of illness, (90% probability interval)	DALY, annual (90% probability interval)
feed (representing water from service line)	$1.14*10^{-7}$ ($1.08*10^{-8}$ to $3.51*10^{-7}$)	$2.49*10^{-16}$ ($1.11*10^{-16}$ to $7.77*10^{-16}$)	$9.10*10^{-14}$ ($4.05*10^{-14}$ to $2.84*10^{-13}$)	$2.00*10^{-13}$ ($8.91*10^{-14}$ to $6.24*10^{-13}$)
water heater (85% of hot water sample at 48 °C and 15% at 60 °C for a final temperature of 49.8 °C)	$2.68*10^{-6}$ ($3.72*10^{-8}$ to $1.10*10^{-5}$)	$5.90*10^{-15}$ ($1.11*10^{-16}$ to $2.36*10^{-14}$)	$2.16*10^{-12}$ ($4.05*10^{-14}$ to $8.63*10^{-12}$)	$4.74*10^{-12}$ ($8.91*10^{-14}$ to $1.90*10^{-11}$)
blend (65% hot at 48 °C and 35% cold water at 25 °C for a final temperature of 40 °C)	$9.70*10^{-7}$ ($4.09*10^{-8}$ to $3.62*10^{-6}$)	$2.14*10^{-15}$ ($1.11*10^{-16}$ to $7.99*10^{-15}$)	$7.80*10^{-13}$ ($4.05*10^{-14}$ to $2.92*10^{-12}$)	$1.72*10^{-12}$ ($8.91*10^{-14}$ to $6.42*10^{-12}$)

Therefore, the daily or per exposure probability equation is rewritten to accommodate this extrapolation

$$P_{inf,\text{daily,pulmonary}} = 1 - e^{-rd/C} \quad (6)$$

where c is the conversion factor estimated at 500 in ref 35.

2.5. Risk Characterization. The inhalation risk for THMs is given by

$$\text{risk} = \text{EC} \times \text{IUR} \quad (7)$$

where EC is the exposure concentration, and IUR is the inhalation unit risk.

The annual risk of MAC illness is calculated with the following equation

$$P_{\text{inf,ann}} = 1 - \prod_{1}^{nf} (1 - P_{\text{inf,daily}}) \quad (8)$$

where n is the number of days on which the exposure occurs, f is the frequency, and $P_{\text{inf,daily}}$ is the daily probability of infection. This assumes that each day is an independent trial, with a constant risk of infection on each day.

DALYs were calculated to compare the health burden of diseases associated with exposures to both MAC and DBPs. Both microbial and chemical risks in this analysis were based on an exposure duration of 1 year (365 days) to enable the comparison of measured DALYs for both exposures to MAC and DBPs. As MAC-specific DALY values are not available, the DALY estimation for the MAC pulmonary disease was based on disability weights and duration of mild chronic obstructive pulmonary disease. This was based on the assumption of similar observed symptoms. The DALY is expressed in the equation

$$\text{DALY} = \text{YLL} + \text{YLD} \quad (9)$$

where YLL is the number of life years lost due to mortality, and YLD is the number of years an individual lived with the disability due to illness. The expected value of YLL is described in the equation

$$E[\text{YLL}] = \text{Prob}[\text{Death|Illness}] \times \text{Prob}[\text{Illness}] \times L_{\text{YLL}} \quad (10)$$

where L_{YLL} is the standard life expectancy at the age of death in years, which is calculated by subtracting the medial age of infection from the standard life expectancy. Probability of death given illness is 1—the survival rate, and the probability of illness is calculated from the dose−response model.

The expected value of YLD is given in the equation

$$E[\text{YLD}] = \text{DW} \times L_{\text{D}} \times \text{Prob}[\text{Illness}] \times (1 - \text{Prob}[\text{Death|Illness}]) + \text{DW} \times L_{\text{L}} \times \text{Prob}[\text{Death|Illness}] \times \text{Prob}[\text{Illness}] \quad (11)$$

where DW is the disability weight, L_{D} is years lived with infection/illness for nonfatal cases based on duration of treatment considering an individual with no underlying issues, and L_{L} is the average duration of fatal cases (years). Sensitivity analysis was conducted to identify which uncertainty in the model inputs contributed the most to the uncertainty in the output. The Spearman rank correlation coefficient was used to identify the most important predictive factors of the annual risk of illness.

3. RESULTS

In Sections 3.2, 3.3, 3.4, 3.5, and 3.6, the results are presented in the following order: the dose, the annual risk, the DALY values, and sensitivity analyses. For both inhalation and ingestion scenarios, comparisons are made between the feed (water from the service line) and the data from the different cold water pipes and the water heater.

3.1. Data Analysis. The concentration data for NTM in water heater tanks are based on the values reported in ref 23. The log-normal distribution was used for the NTM concentration, and the results from the nonparametric test of significance indicated no significant difference between the different stagnation times, high-use (three times per day) and low-use (once per day), and the different water heater shower temperatures, 48 and 60 °C.

The analyses of TTHM concentrations in hot water storage tanks are reported in ref 31. The results indicated no significant impact of water use frequency and water heater temperature on TTHMs and HAAs. The data analyses for TTHM and HAA concentrations in the cold water storage tanks are reported in ref 33. The ANOVA results indicated that the pipe material had a significant impact on the mean TTHM concentrations ($p = 0.05$), while the water use frequency, pipe material, and the interaction between the water use frequency and pipe material significantly impacted the mean HAA concentrations. The effect of the pipe diameter was not significant for either set of DBPs. For the analysis of censored data, in cases where the NTM concentrations are below the limit of detection (LD), the replacement method with half the limit of detection (LD/2) was utilized.[40] For the DBP data, 100% of the THM and HAA concentrations were observed to be above the detection limit, and no substitution was required.

3.2. Risk Characterization of MAC via Inhalation. Table 2 summarizes the average daily exposure dose, daily probability of illness, annual risk, and DALY estimation based on the feed concentration, the water heater concentration

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(data from different temperatures and stagnation times were pooled), and blended hot and cold (65% hot and 35% cold) water concentrations from the Monte Carlo simulation. The average daily dose of MAC concentration estimated from the service line (feed), the hot water data, and the blended shower was $1.14*10^{-7}$, $2.68*10^{-6}$, and $9.70*10^{-7}$ cfu, respectively.

For each shower temperature, the average annual risk did not exceed the commonly cited annual risk benchmark of $1*10^{-4}$. The average annual risks for the feed, hot water, and blended shower water were $9.10*10^{-14}$, $2.16*10^{-12}$, and $7.80*10^{-13}$, respectively. The DALY values estimated for MAC pulmonary disease burden were $2.00*10^{-13}$ for the feed, $4.74*10^{-12}$ for the water heater data, and $1.72*10^{-12}$ for the blended shower, which are well below the common benchmark for the acceptable DALY associated with drinking water supplies of $1 * 10^{-6}$ DALY per year.[41]

The model inputs with probabilistic distributions for sensitivity analysis include the exposure time, breathing rate, the enrichment factor, and MAC concentration. The model inputs were ranked based on their correlation coefficient with the output variable. For the risk analysis conducted using the feed water, the most predictive input factors were the enrichment factor (rho = 0.63) and MAC concentration in water (rho = 0.52). The other inputs such as the shower time (rho = 0.38) and the breathing rate (rho = 0.08) all had weak correlation with the output. For the analysis using the water heater data (based on the weighted average consisting of 85% of the values at 48 °C and 15% of the values at 60 °C), the most important factor was the MAC concentration in water (rho = 0.84), while the enrichment factor (rho = 0.39), the shower time (rho = 0.24), and the breathing rate (rho = 0.06) all had weak correlation with the annual risk of illness. For the blended shower, the most predictive input was also the MAC concentration in water (rho = 0.85), while the enrichment factor (rho = 0.37), the shower time (rho = 0.23), and the breathing rate (rho = 0.05) were all less strongly correlated with the annual risk of illness. Sensitivity analysis found that the enrichment factor had the greatest impact on the risk of MAC pulmonary disease and DALYs given the wide range of uncertainty. Increasing the enrichment factor from 125 to 9871 increased the annual risk by 2 orders of magnitude from $4.40*10^{-15}$ to $6.93*10^{-13}$. Also, an increase in the concentration of MAC in the bulk water for the blended shower waters from $6.87*10^{-5}$ to 1.24 (cfu/m^3) increased the annual risk from $2.48*10^{-18}$ to $1.66*10^{-10}$, and an increase in the shower time from 5 to 25 min increased the annual risk from $2.16*10^{-13}$ to $1.31*10^{-12}$.

3.3. Risk Characterization of THMs via Inhalation. The average exposure concentrations of THM estimated by the Monte Carlo analysis from the service line (feed), blend, and water heater data were $4.54*10^{-3}$, $4.69*10^{-3}$, and $4.82*10^{-3}$ mg/m^3, respectively. The average annual TTHM risks for the feed, blend, and water heater data were $1.24*10^{-7}$, $1.25*10^{-7}$, and $1.30*10^{-7}$, respectively. The lifetime cancer risk benchmark is usually in the 1 in a million to 1 in 10,000 range, which may indicate an annual range considering a lifetime of 70 years as $1.43*10^{-8}$ ($10^{-6}/70$) to $1.42*10^{-6}$ ($10^{-4}/70$). If considering the 1 in a million benchmark, the average risk measured in the feed, blend, and water heater data were higher than the risk benchmark, but if considering the lifetime 1 in 10,000 benchmark, the average risks were an order of magnitude lower than the benchmark. The DALYs for TTHMs estimated for bladder cancer burden were $7.31*10^{-7}$ for the feed, $7.40*10^{-7}$ for the blend, and $7.61*10^{-7}$ for the water heater data. Overall, CFM, BDCM, DBCM, and BFM contributed to 44.6−49.3, 27.1−32.8, 21.2−23.4, and 1.53−1.57% of average cancer risk, respectively.

For each of the THM species considered, the most important factor on the annual risk of illness based on the Spearman rank correlation was the concentration of the THM species in the air with an average rho value of 0.93, the exposure time (rho = 0.82), and the shower volume (rho = −0.51). The concentration in water was the least important factor (rho = 0.14). For the blended scenario, an increase in the shower time from 5 to 25 min increased the total TTHM annual risk by an order of magnitude from $1.26*10^{-8}$ to $2.98*10^{-7}$. The nonlinear relationship reflects that both the air concentration and duration of exposure increase with a longer shower duration. Increasing the shower volume from 2 to 18 m^3 decreased the total TTHM annual risk by an order of magnitude from $4.22*10^{-7}$ to $5.26*10^{-8}$.

3.4. Chemical Cancer Risk for THMs via Ingestion. The chronic daily doses for THMs via ingestion of the feed was $3.53*10^{-6}$ mg/m^3, and the average annual dose in the pooled building cold water data was $3.63*10^{-6}$ mg/m^3. The average annual risk of TTHM illness in the feed was estimated at $1.75*10^{-7}$, and the average annual risk in the pooled cold water data was just slightly higher at $1.79*10^{-7}$. The DALYs estimated in the feed and the pooled data were $2.56*10^{-6}$ and $2.62*10^{-6}$, respectively, which are greater than the target DALY threshold of 1μDALY. For the different pipe materials, PVC, PEX, and copper, the annual dose of total THM was slightly higher in copper ($3.70*10^{-6}$) than in PVC ($3.64*10^{-6}$) and PEX ($3.53*10^{-6}$).

The annual risk and DALYs followed the order copper > PVC > PEX, with the annual risk values of $1.83*10^{-7}$, $1.80*10^{-7}$, and $1.75*10^{-7}$, respectively, and the DALY values of $2.69*10^{-6}$, $2.64*10^{-6}$, and $2.56*10^{-6}$, respectively. Differences by water use frequency, between high (every 12 h) and low (every 7 days), were not statistically significantly different, although the annual dose, annual risk, and DALY values were higher in the low-use pipes than in the high-use pipes. The annual risk was $1.80*10^{-7}$ in the low-use pipes and $1.78*10^{-7}$ in the high-use pipes. Overall, BDCM, DBCM, CFM, and BFM contributed to 51.3−51.6, 40.3−40.5, 7.12−7.18, and 1.02−1.02% of the average annual risk, respectively. In each scenario considered, the annual risk exceeded the more protective target for the acceptable annual cancer risk threshold ($1*10^{-6}/70 = 1.4*10^{-8}$) and the less stringent target ($1 *10^{-4}/70 = 1.4*10^{-6}$). The Spearman rank correlation indicated that the ingestion rate (rho = 0.94) was the most important uncertainty, while the THM concentration in water was the least important uncertainty (rho = 0.29) influencing the annual risk of THM illness. The Mann−Whitney U test indicated no statistical difference between the risk of THM based on the feed data and the building pooled data ($p < 0.01$).

3.5. Chemical Cancer Risks for HAAs via Ingestion. The chronic daily doses, the annual risk, and the DALY values estimated in the feed were almost always higher than those estimated in the different premise plumbing conditions, reflecting the possible biodegradation of HAAs in the building plumbing. The chronic daily doses for the total HAAs (DCAA, TCAA, and DBAA) via ingestion exposure estimated in the feed was $8.13*10^{-4}$ mg/kg day, and the average annual dose in the pooled building data was $4.26*10^{-4}$ mg/kg day. The

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average annual risk of HAAs in the feed was estimated at $2.50*10^{-7}$, and the average annual risk in the pooled building data (all pipe samples) was $1.77*10^{-7}$. The DALYs estimated both in the feed and the pooled data were $3.68*10^{-6}$ and $2.60*10^{-6}$, respectively, which are greater than the DALY threshold of 1μDALY. For the different pipe materials, PVC, PEX, and copper, the annual dose of total HAAs was significantly higher in copper ($2.26*10^{-6}$) than in PVC ($2.06*10^{-6}$) and PEX ($1.79*10^{-6}$), possibly due to the decreased biodegradation in the copper pipe due to the antimicrobial properties of copper.

The average annual risk and DALYs followed the order copper > PVC > PEX, with the risk values of $1.95*10^{-7}$, $1.78*10^{-7}$, and $1.55*10^{-7}$, respectively, and the DALY values of $2.87*10^{-6}$, $2.60*10^{-6}$, and $2.27*10^{-6}$, respectively. For the different water use frequencies, high (every 12 h) and low (every 7 days), the annual dose, risk, and DALYs of HAAs estimated in the high-use pipes were significantly higher than those in the low-use pipes. The annual risk was $2.27*10^{-7}$ in the high-use pipes and $1.23*10^{-7}$ in the low-use pipes. Overall, DBAA, TCAA, and DCAA contributed to 39.8−40.2, 34.6−34.8, and 25.2−25.4% of the average annual risk, respectively. In each scenario considered, the annual risk exceeded the acceptable annual cancer risk threshold (both the lower bound of $1*10^{-6}/70 = 1.4*10^{-8}$ and the upper bound of $1*10^{-4}/70 = 1.4*10^{-6}$). The Spearman rank correlation for the feed data indicated that ingestion rate was the most important uncertainty factor that influenced the risk of HAA illness via ingestion (rho = 0.88), and the least important factor was the HAA concentration in water (rho = 0.45). On the other hand, the Spearman rank correlation of the building pooled data indicated that the HAA concentrations in water was the most important uncertainty factor influencing the annual risk of HAA illness (rho = 0.81), and the least important uncertainty factor was the ingestion rate (rho = 0.56). These results reflect the greater variability of concentrations in the building pipes compared to the variability in the feed water. The variability in the building water was in large part due to the long range of stagnation times (12 h to 1 week) which allowed a variation in the amount of biodegradation.

3.6. Chemical Cancer Risk via Dermal Absorption. For the total THMs, the chronic daily doses, the annual risk, and the DALY values estimated in the feed were slightly higher than those estimated in the blended shower and water heater data, whereas for the total HAAs, the dose, annual risk, and DALY values were lower in the feed than in the blended and water heater shower data. The chronic daily doses for the total THMs in the feed, blended shower, and water heater data were $3.55*10^{-8}$, $3.53*10^{-8}$, and $3.51*10^{-8}$ (mg/kg day), respectively. The chronic daily doses for the total HAAs (DCAA, TCAA, and DBAA) estimated in the feed, blended, and water heater shower data were $5.86*10^{-9}$, $5.92*10^{-9}$, and $6.07*10^{-9}$ (mg/kg day), respectively.

The average annual TTHM risks for the feed, blend, and water heater data were $1.56*10^{-9}$, $1.55*10^{-9}$, and $1.55*10^{-9}$, respectively. The average annual HAA risks for the feed, blend, and water heater data were $3.92*10^{-10}$, $3.96*10^{-10}$, and $4.07*10^{-10}$, respectively. The annual risks estimated via dermal absorption for both TTHMs and HAAs were lower than the usual annual cancer risk benchmark within the range of $1.43*10^{-8}$ ($10^{-6}/70$) to $1.42*10^{-6}$ ($10^{-4}/70$). The DALYs for TTHMs estimated for bladder cancer were $9.21*10^{-9}$ for the feed, $9.18*10^{-9}$ for the blend, and $9.14*10^{-9}$ for the heater data. For the HAAs, the DALY values were $2.32*10^{-9}$, $2.34*10^{-9}$, and $2.40*10^{-9}$ for the feed, blend, and water heater data, respectively. For the total THM cancer risk, CFM, BDCM, DBCM, and BFM contributed to 43.1−43.3, 35.9−36.1, 20.3−20.4, and 0.42% of average cancer risk, respectively. For the total HAA cancer risk, TCAA, DCAA, and DBAA contributed to 54.6−55.1, 33.1−33.5, and 11.9% of average cancer risk, respectively. For each of the THM and HAA species considered, Spearman correlation coefficients indicated that the most important factor for the annual risk was the exposure time. For THMs, the correlation coefficient value rho = 0.91, and for HAA, rho = 0.87.

The annual risks and DALY values estimated from the ingestion routes for TTHMs closely match those estimated for THAAs. For TTHMs, risk from ingestion is somewhat higher than the risk from inhalation, but both are roughly on the same order of magnitude. For TTHMs, dermal risks are substantially lower than inhalation and ingestion risks. MAC risks are lower than the TTHM and THAA risks. Overall, drinking water ingestion is associated with greater risk than showering. This is because drinking water exposes individuals to TTHM and THAA ingestion risks, which are both on the order of 10^{-7}. In contrast, showering involves exposure to only one risk on the order of 10^{-7}, and TTHM inhalation risks (MAC inhalation, TTHM dermal, and THAA dermal risks) are orders of magnitude lower. Table 3 compares the annual risk and DALY for the different exposure routes - inhalation, dermal contact, and ingestion.

4. DISCUSSION

4.1. Comparing Health Burdens and Risks from Exposure to Chemical and Microbial Contaminants. To the author's knowledge, this study is the first to quantitatively compare microbial and chemical risks in building plumbing using the annual risk and DALY approaches for a general population. An earlier study compared microbial and chemical risks in drinking water but did not address on how changes in concentrations in building plumbing influence risks.[20] They used the DALY concept and found that the health benefits of preventing gastroenteritis caused by *Cryptosporidium parvum* in the general population and premature death in patients with acquired immunodeficiency syndrome outweigh the health losses by premature death from renal cell cancer by a factor of more than 10, suggesting that the microbial contamination of water supplies pose a clear public health risk when *Cryptosporidium* is present. An overview by ref 9 further suggests that an effort to reduce the potential health risks from DBPs must not compromise the pathogen control. However, in this study, the health burdens estimated using the DALY approach indicated that bladder cancer risk from THM exposure outweighs MAC pulmonary disease from MAC infection at least for the general population, considering showering as an exposure scenario in buildings. The annual probability of illness and health burdens (DALYs) of MAC pulmonary disease for the general population via inhalation during showering were lower than those from bladder cancer by 5 orders of magnitude. The annual risks of MAC pulmonary disease estimated from showering (10^{-12}) were lower than the annual microbial risk threshold of 10^{-4}. Similarly, the daily risks of MAC illness (10^{-15}) were generally lower than the daily risk threshold of 10^{-7}. On the other hand, the annual chemical risks of DBPs estimated via inhalation and ingestion were higher than the annual chemical risk threshold

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Table 3. Annual Risk and DALY Values for MAC (Inhalation), TTHM (Inhalation, Dermal Contact, and Ingestion), and THAA (Dermal Contact and Ingestion) in Water Heater (MAC, THAA, and TTHM Inhalation and Dermal Contact) and Pooled Cold Water Data (THAA and TTHM Ingestion)

	inhalation		dermal contact		ingestion	
	MAC (90% probability interval)	TTHM (90% probability interval)	THAA (90% probability interval)	TTHM (90% probability interval)	THAA (90% probability interval)	TTHM (90% probability interval)
annual risk	$2.16*10^{-12}$ ($4.05*10^{-14}$ to $8.63*10^{-12}$)	$1.30*10^{-7}$ ($1.19*10^{-8}$ to $4.10*10^{-7}$)	$4.07*10^{-10}$ ($1.24*10^{-10}$ to $8.24*10^{-10}$)	$1.55*10^{-9}$ ($5.98*10^{-10}$ to $2.67*10^{-9}$)	$1.77*10^{-7}$ ($6.18*10^{-8}$ to $3.66*10^{-7}$)	$1.79*10^{-7}$ ($9.63*10^{-8}$ to $2.70*10^{-7}$)
DALY	$4.74*10^{-12}$ ($8.91*10^{-14}$ to $1.90*10^{-11}$)	$7.61*10^{-7}$ ($7.04*10^{-8}$ to $2.42*10^{-6}$)	$2.40*10^{-9}$ ($7.35*10^{-10}$ to $4.87*10^{-9}$)	$9.14*10^{-9}$ ($3.53*10^{-9}$ to $1.58*10^{-8}$)	$2.60*10^{-6}$ ($1.27*10^{-6}$ to $5.52*10^{-6}$)	$2.62*10^{-6}$ ($1.41*10^{-6}$ to $3.96*10^{-6}$)

of $1.4*10^{-8}$ (considering the 1 in a million benchmark on an annual basis). Results from recent studies have also indicated lower risk of microbial exposure and higher risks of chemical exposure. A study by ref 42 reported lower risk of pulmonary infections caused by *Mycobacterium* spp. via showering. They reported that the median risks of pulmonary infections estimated from inhalation exposures were all 2.4×10^{-9} or lower, which were all lower than the daily risk threshold of 10^{-7}. Some studies on chemical cancer risk exposure reported that the cancer risk values of THMs via inhalation during showering were higher than the 10^{-6} benchmark, based on the lifetime calculation of cancer risk.[43−45] In comparing the risks of illness from MAC and DBPs, the results from this study indicate that despite the growing concern of risks associated with the potential exposure to opportunistic pathogens and the general consideration of pathogens posing a higher risk than chemicals,[46,47] the higher disease burden of bladder cancer from exposure to THMs than MAC pulmonary disease may suggest that efforts to reduce potential health risks from DBPs should still be given due consideration at least for the general population and to exposures in this specific building plumbing scenario. It is notable that *Legionella* were not detected in this system, but when present, *Legionella* might substantially increase the microbial risk. While these results are specific to the system studied (chloramine building water supply, mid-Atlantic location, electric water heaters, etc.) and the data collected (*Legionella pneumophila* were never detected in either cold or hot water experiments), the framework developed here presents a method to evaluate how plumbing systems influence microbial and chemical risks.

4.2. Combined Annual Risks of Inhalation and Dermal Exposures during Showering are Comparable to Ingestion for Chemical Cancer Risk. In this study, the combined annual risk of THM via inhalation and dermal absorption during an average shower time of 15 min ($1.30*10^{-7} + 1.55*10^{-9} = 1.31*10^{-7}$) was comparable to the annual risk of daily consumption of 2.0 L of drinking water via ingestion ($1.79*10^{-7}$). This observation is consistent with the findings from Jo and Weisel[48] that reported that the estimates of chloroform risk from showering (inhalation and dermal) were comparable to the estimates from daily water ingestion. They reported that the risk associated with a single 10 min shower was estimated to be $1.22*10^{-4}$, while the estimated risk from daily ingestion of tap water ranged from $1.30*10^{-5}$ to $1.80*10^{-4}$. In this study, it was also observed that dermal absorption alone is not as important as inhalation and ingestion. The annual risks of drinking tap water via ingestion and the combined risk via inhalation and dermal absorption of THMs were higher than the annual benchmark range of 10^{-8} to 10^{-6} (based on the 10^{-6} to 10^{-4} annual benchmarks). This indicates that both showering and consumption of tap water are important exposure routes. Dermal infections from NTM which are primarily a concern for NTM other than MAC were not considered in this analysis, but it warrants further research.

4.3. Influence of Building Plumbing Design and Operational Parameters on Microbial and Chemical Risks. The results from this study showed that the risk of TTHM ingestion based on the feed data differed only modestly from the risk based on the cold water pipe data for an ingestion exposure scenario. This suggests that building water system has only limited influence on the risk of THMs via ingestion. The risk of HAAs via ingestion based on the cold water pipe data was lower than the risk of HAAs in the feed

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service line water, with the lowest risks found in the pipes with the longest stagnation times. The lower concentrations of HAAs in the pipes support the hypothesis that HAAs undergo microbial degradation.[49−51] THM formation occurs in pipes, but substantial formation appears to be associated with free chlorine systems.[4,52,53] Another study reported higher levels of THMs in buildings up to 89% higher than the levels found at the service line.[52] However, in the chloramine system considered here, the effects of residence in the building plumbing system appear to be relatively modest and somewhat beneficial (as HAAs are degraded).

The feed scenario water quality is not impacted by the building plumbing system, while the water quality in the blend water heater and cold water pipe scenarios is influenced by the building plumbing system. Chemical risks in the feed versus the other scenarios (blend, water heater, and cold water pipe) are roughly on the same order of magnitude. In the longer stagnation duration samples, DBP risk was modestly attenuated by the decreased exposure to THAAs. However, microbial risks vary greatly from the feed, with the blend and water heater scenarios having an order of magnitude higher risks than the feed. In summary, the plumbing system increased microbial risks relative to the feed but modestly decreased DBP risks due to the degradation of THAAs in the building plumbing. While the relative importance of microbial versus DBP risks could be dramatically different in a *Legionella*-positive system, or when vulnerable populations are considered, the overall framework presented here provides a basis for prioritizing among these risks.

A limitation of this study is that the intensive sampling required to characterize both microbiological and chemical risks limited the number of conditions that could be characterized. Future efforts to better understand microbial versus chemical risks are warranted, including the consideration of conditions where *Legionella* are present. Another limitation to this study is the exclusion of unregulated DBPs from this analysis. This study focused on trade-offs in regulated DBPs and mycobacteria as they have not been addressed adequately or quantitatively in prior studies. The comparative analysis for MAC in this study did not include the ingestion route which is the route of concern for MAC exposure in immunocompetent individuals and is also a limitation of this study. Additionally, culture-based methods may omit viable but nonculturable microorganisms. To the extent that the ratio of culturable versus total infectious organisms is not constant, this variation becomes an additional uncertainty of our analysis. Future works should address how alternatives to culture, including direct count, viability-based qPCR, and so forth may be used to better understand the true quantity of infectious organisms. This study relied on periodic sampling that may miss rare, high-exposure events. Such exposures might occur after long stagnation times (return from vacation, etc.) or other conditions (loss or residual in building supply, favorable temperatures) which lead to high levels of opportunistic pathogens in building plumbing. Future efforts to identify these low-frequency but high-risk events are warranted.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsestwater.2c00019.

Concentration data of MAC, THMs, and THAAs for the different exposure scenarios and model input and output parameters for Monte Carlo exposure assessment for microbial and cancer risk assessment and DALY calculations (PDF)

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Notes

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